ENDOCRINE GLANDS I
Pituitary & Pineal

ENDOCRINE GLANDS

In multicellular organisms intercellular communication between the cells of each organ, and between different organs is necessary to maintain:

1. **homeostasis of nutrients & vital substances in the cellular environment.**
2. **coordination of growth and development.**
3. **adaptation to environmental stresses.**

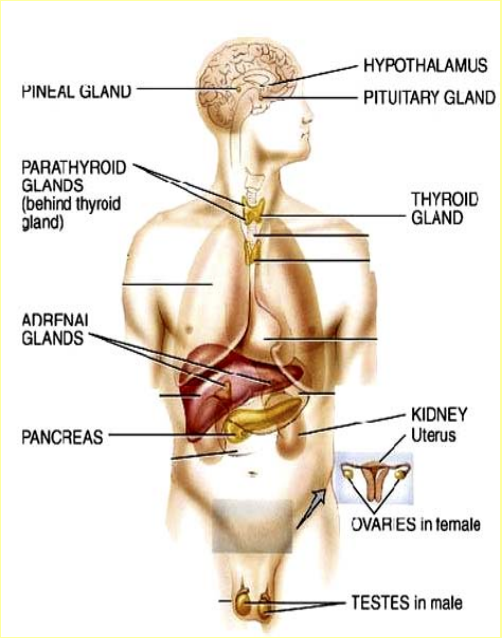
Two communication systems have evolved to meet these needs:

A. The Nervous System: (fast acting, specific targets through specific channels)

B. The Endocrine System: (slower acting, more pervasive, some degree of target specificity)

THE ENDOCRINE SYSTEM

Composed of ductless glands whose secretions (*hormones*) are passed directly to the blood or lymph circulation for transport to distant target organs.



Traditionally there are 8 endocrine glands:

Pituitary -- Thyroid -- Parathyroid -- Adrenals

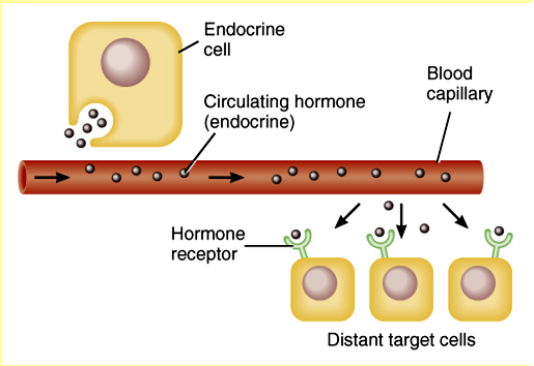
-- Pancreatic Islets -- Pineal -- Testis -- Ovaries

Hormone:

is an organic compound secreted in small amounts by endocrine cells which exerts its effect on distant target tissues or organs.

Hormones can have different sites of action:

Circulating Hormones: effects at a distance



Circulating:

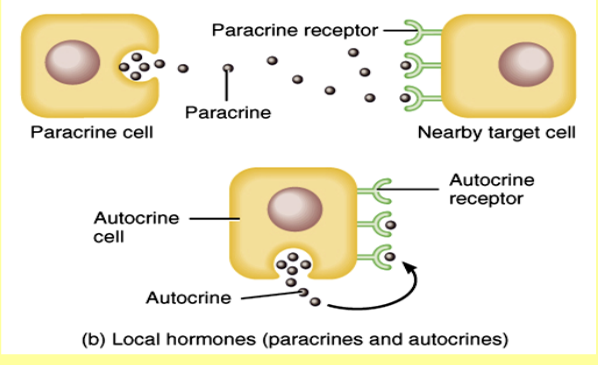
- **acts on distant target tissues**
- **travel via the circulatory system**

Local

- **Paracrine**
  act on neighboring cells and tissues

- **Autocrine**
  act on the same cells that secrete them

Local Hormones: short-range effects



Over 100 distinct Hormones have been identified as products of endocrine cells.

Chemically these are divided into 3 classes:

1. **Steroid Hormones**
   adrenal cortical hormones – testosterone - estrogen, progesterone

2. **Protein Hormones - growth hormone - prolactin, (glycoproteins)**

3. **Amino Acid Derivatives - norepinephrine, thyroxine**

PROPERTIES OF HORMONE ACTION

SPECIFICITY:

- **exhibit specific effects -- "activation or inhibition" of target organs which possess specific receptors sites for the hormone.**

LOW CONCENTRATION:

- **typically effective at very low concentrations (10^{-7}M - 10^{-12} M)**

FEEDBACK CONTROL:

- **Once a hormone has exerted its effect on the target organ, information is transferred either directly or indirectly back to the endocrine organ to regulate further secretion.**

TIME COURSE:

- **There is wide variation in the time course over which given classes of hormones exert their effects.**

- **Peptides = seconds Proteins = hours Steroids = days**

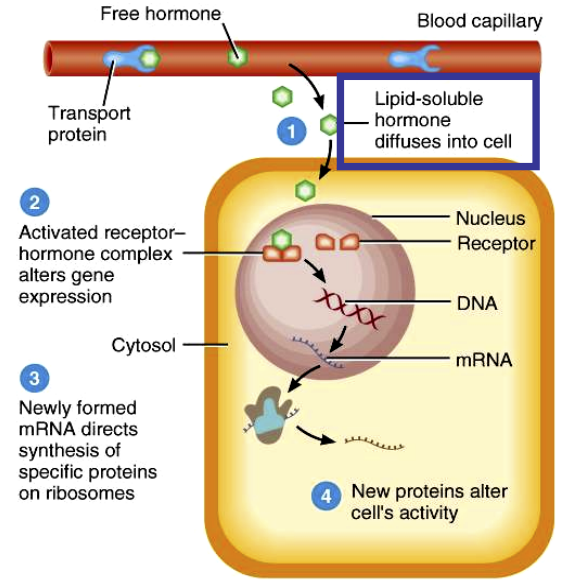
Hormones exert their effects on target cells in 2 ways

1. Directly (lipid soluble hormones)

- Hormone diffuses through phospholipid bilayer & into cell
- Binds to receptor turning on/off specific genes
- New mRNA is formed & directs synthesis of new proteins

- by incorporation into the cell membrane, cytoplasm or nucleus to modulate membrane permeability, gene expression or protein synthesis.

- Lipid soluable hormones (steroids) typically utilize this mode



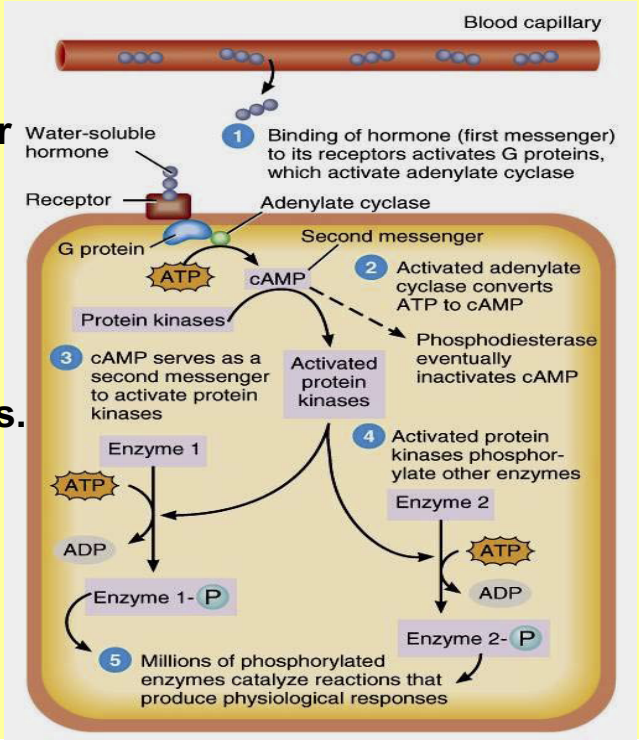
2. Indirectly (aqueous soluble hormones)

hormone binds to a membrane receptor – hormone + receptor complex activates a membrane bound enzyme (adenylate cyclase)

- the activated enzyme catalyses the production of an intracellular "second messenger" (cAMP).

- second messenger initiates an Intracellular signalling cascade which mediates the effects of the hormone on the target organs.

- This mode is typically utilized by peptide hormones.



Embryological Origins of Endocrine Tissues

- **The endocrine glands vary in their embryological origins.**

- **As a group they are derived from all three embryonic germ layers:**

  1. ***Ectoderm*: Pituitary - Adrenal Medulla - Pineal - Enterochromaffin cells**

  2. ***Mesoderm*: Adrenal Cortex - Testis - Ovaries**

  3. ***Endoderm*: Islets of Langerhans - Parenchymal cells of Thyroid & Parathyroid**

STRUCTURE OF ENDOCRINE GLANDS

Simple histological structure consisting of

- **plates or cords of parenchymal cells**

- **separated by fenestrated sinusoids supported by delicate connective tissue framework (reticular fibers).**

- **Endocrine tissues are highly vascularized by permeable fenestrated capillaries or sinusoids into which their hormonal secretions are emptied.**

TYPES OF ENDOCRINE TISSUE

- **The endocrine components of the body occur in 3 basic forms:**

1. **<u>distinct aggregates</u> of hormone secreting cells**
   [endocrine organs: pituitary - thyroid - parathyroid - adrenal - pineal]

2. **<u>Isolated endocrine cells:</u>**
   principally in within the epithelial lining of the gastrointestinal system and respiratory tracts
   (Enterochromaffin cells of the diffuse neuroendocrine system)

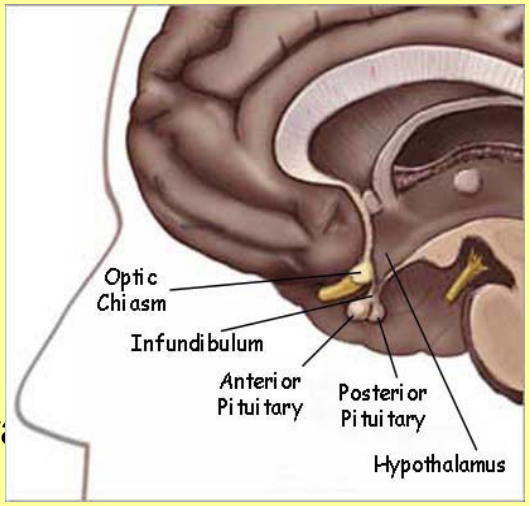
3. **<u>Scattered masses</u>: of endocrine tissue distributed within exocrine glands or other organs**

Leydig cell of the Testis - Corpora Lutea of the Ovary - Juxtaglomerular cells of the Kidney -- Islets cells of the Pancreas

PITUITARY GLAND

Referred to as the "Master Gland" due to its critical role in producing and regulating the secretions of the major hormones of the body

- **Pituitary acts in concert with the Hypothalamus of the CNS, to exert precise control over the plasma levels of hormones**



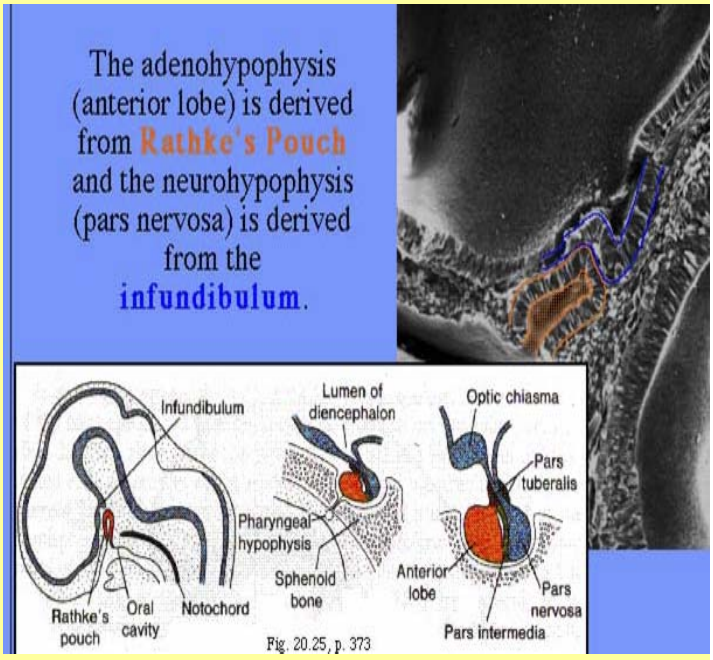
STRUCTURE:

- **A small oval structure (1 x 1.5 cm) attached by infundibular stalk to the undersurface of the hypothalamus. Covered by connective tissue capsule (dura = Diaphragma Sellae.**

EMBRYOLOGY:

Embryologically the pituitary develops from two sources:

1. **an upgrowth of epithelial tissue from the roof of the oral ectoderm (Rathke'sPouch) = *ADENOHYPOPHYSIS***



2. **A downgrowth of neuroectoderm from the hypothalamus of the CNS = *NEUROHYPOPHYSIS***

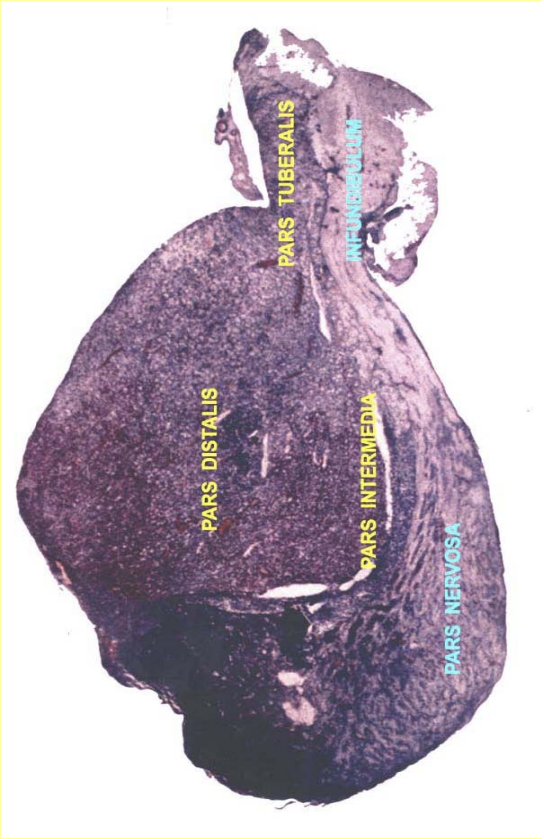
The pituitary can be divided into 4 parts:

1. ***PAR DISTALIS***:
   - largest and anterior portion

2. ***PARS TUBERALIS***:
   arises from the pars distalis
   to wrap around the infundibular stalk

3. ***PARS INTERMEDIA***
   thin cellular partition separating
   the pars distalis from the pars nervosa
   - present in some mammals but
   vestigial in humans

4. **PARS NERVOSA**
   - specialized neuroendocrine tissue
   attached to the *median eminence* of the
   tuber cinereum of the hypothalamus



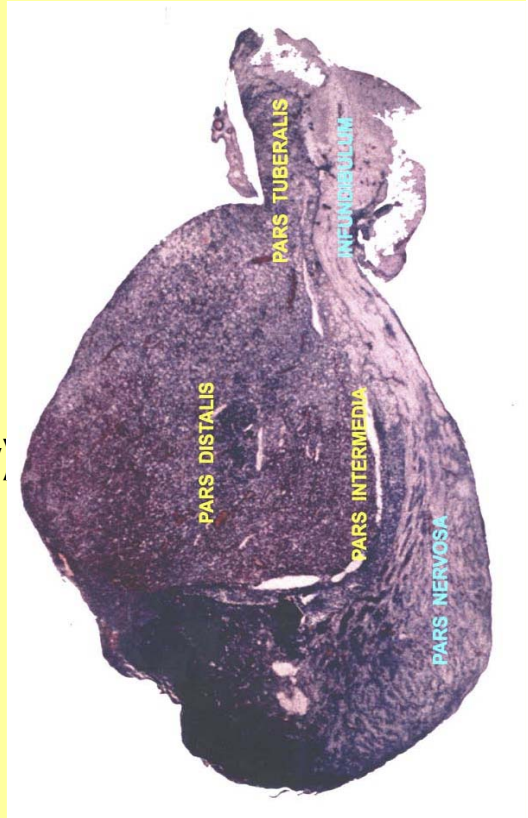
More commonly the pituitary is simply divided into an:

Anterior Lobe (anterior pituitary)

- **pars distalis + pars tuberalis + pars intermedia**

Posterior Lobe (posterior pituitary)

- **pars nervosa + Infundibulum + median eminence**



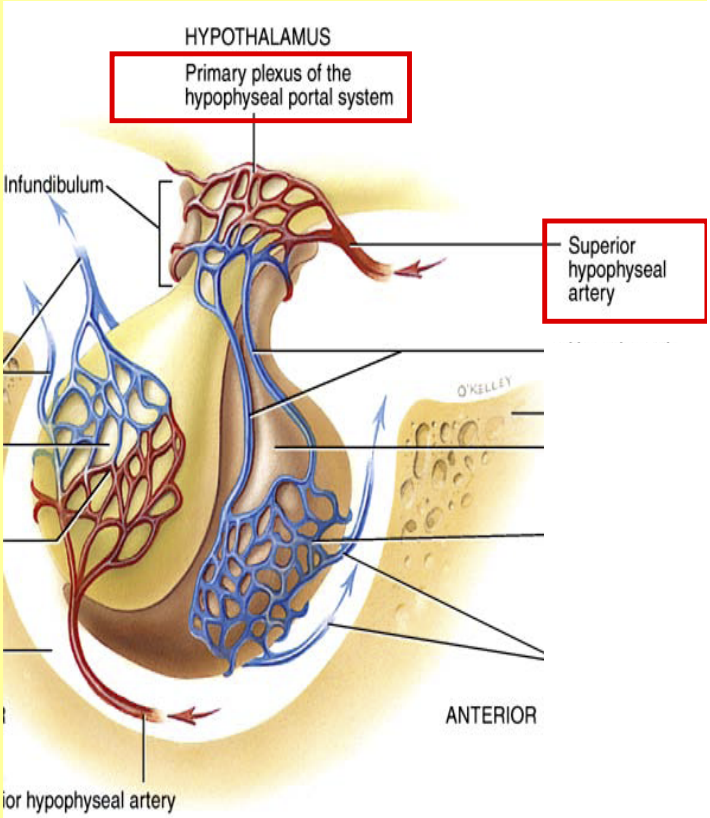
BLOOD SUPPLY OF THE PITUITARY

Knowledge of the blood supply of the pituitary is critical to understanding the pattern of distribution of its hormones.

THE ANTERIOR LOBE:

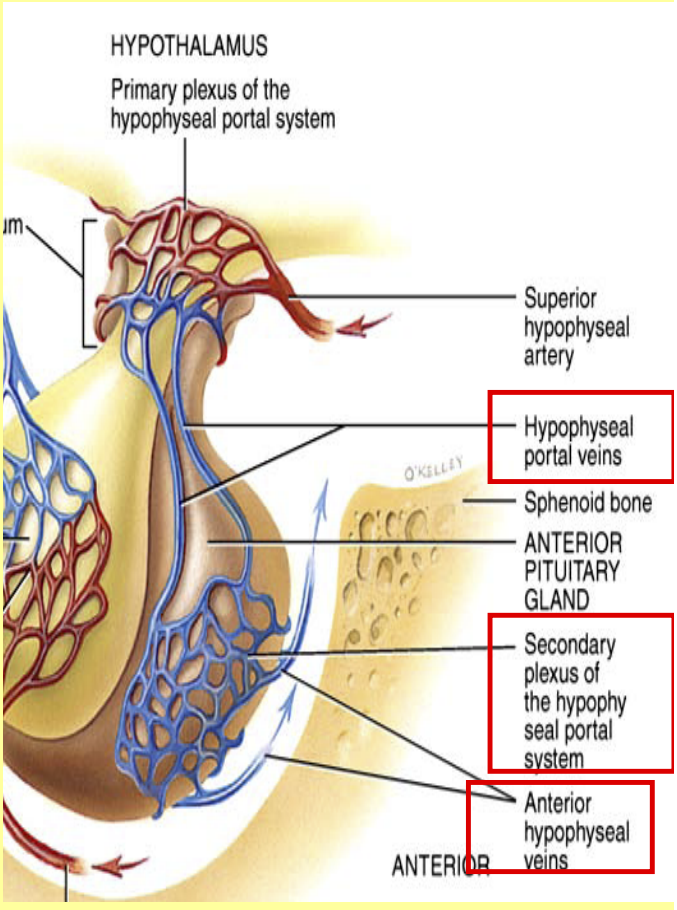
- **The blood supply of the anterior lobe is derived from several *superior hypophyseal arteries* which arise from the internal carotids.**

- **These anastomose freely in the upper portion of the pituitary stalk in the region of the median eminence where they give rise to an extensive "fenestrated" capillary plexus termed the *PRIMARY PLEXUS***



- **The primary plexus empties into a series of long *PORTAL VEINS* which descend in the pituitary stalk to the anterior lobe where they branch extensively**

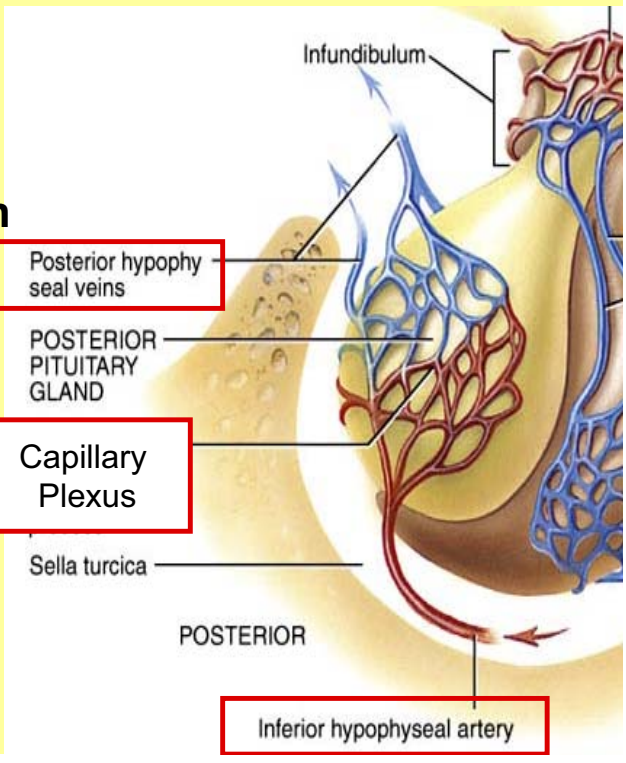
These give rise to a dense *sinusoidal capillary plexus* the *SECONDARY PLEXUS*, which drains by a series of inferior (anterior) hypophyseal veins into the cavernous sinus.



- **The primary plexus, together with the portal veins and secondary plexus are collectively known as the *HYPOTHALAMIC HYPOPHYSEAL PORTAL SYSTEM***
- **This system is the primary vehicle by which "regulatory peptides" from the hypothalamus are distributed to the anterior lobe.**
- **In response to these regulatory peptides, the cells of the anterior lobe empty their hormones into the secondary plexus to be distributed via the circulatory system to their various target organs.**

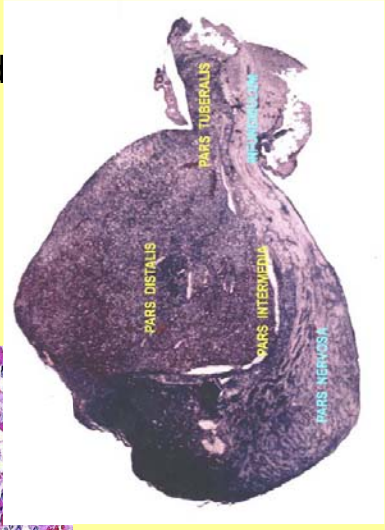
BLOOD SUPPLY OF THE POSTERIOR LOBE:

- **The blood supply of the posterior lobe is derived from a pair of *INFERIOR HYPOPHYSEAL ARTERIES* which also arise from the internal carotids.**
- **These anastomose freely in the parenchyma of the posterior lobe to form a dense capillary plexus which empties into the posterior hypophyseal veins**



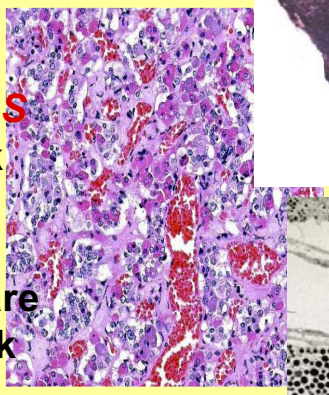
STRUCTURE OF THE ADENOHYPOPHYSIS:

Pars Distalis – Pars Tuberalis – Pars Intermed



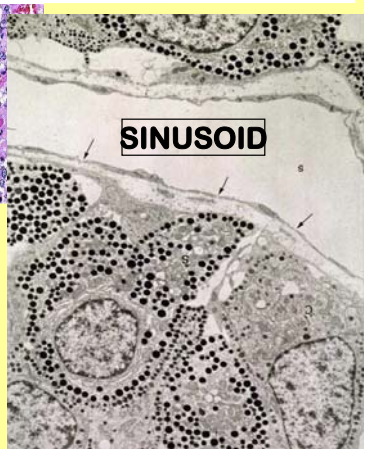
Pars Diatalis

- **Comprises about 75% of the entire pituitary.**



- **dense cords of *SECRETORY EPITHELIAL CELLS* supported by a delicate network of *RETICULAR FIBERS*.**

- **Between the secretory cells are interdigitated a complex network of SINUSOIDAL CAPILLARIES.**



- **Sinusoids are lined by endothelial cells which are FENESTRATED w/ DIAPHRAMS.**

Several types secretory cells of the Pars Distalis synthesize a wide variety of hormones which are secreted into the systemic circulation by way of these fenestrated capillaries.

The 6 most prominent and well studied.

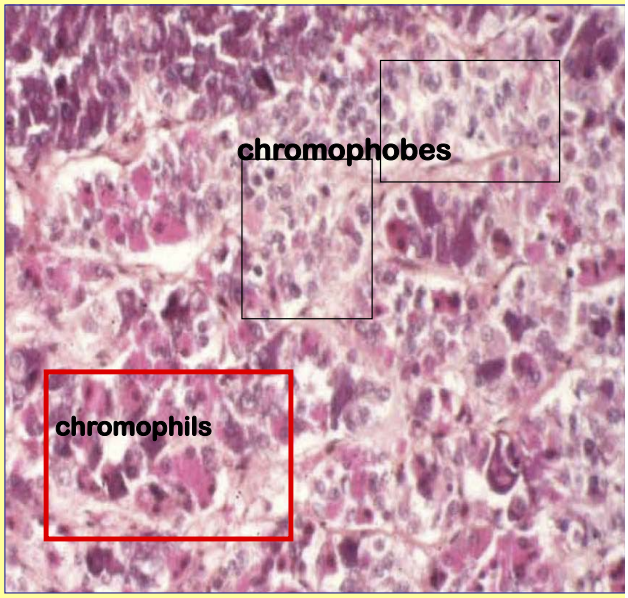
1. **Somatotropin (GH)**
2. **Prolactin (LTH)**
3. **Follicle Stimulating Hormone (FSH)**
4. **Leuteinizing Hormone (LH)**
5. **Thyroid Stimulating Hormone (TSH)**
6. **Adrenocorticotropic Hormone (ACTH)**

PARS DISTALIS CELLS:

- The secretory epithelial cells of the Pars Distalis can be divided into 2 classes based on the avidity with which they accumulate common histological stains.

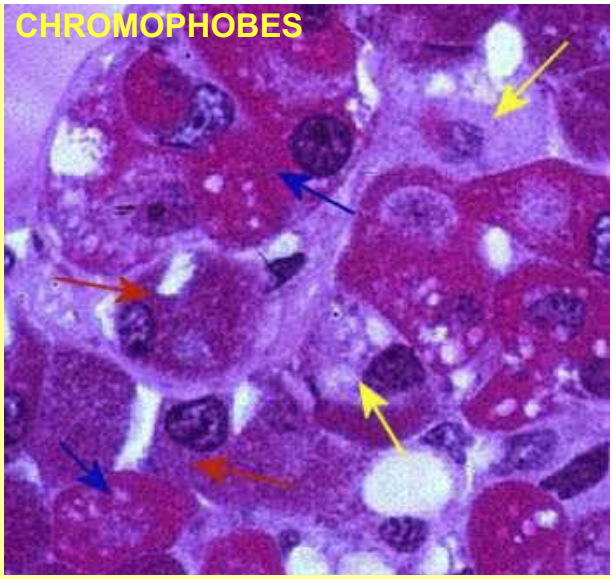
  Chromophobes — Chromophils

- Chromophils consists of several cell types based on the hormones they secrete.

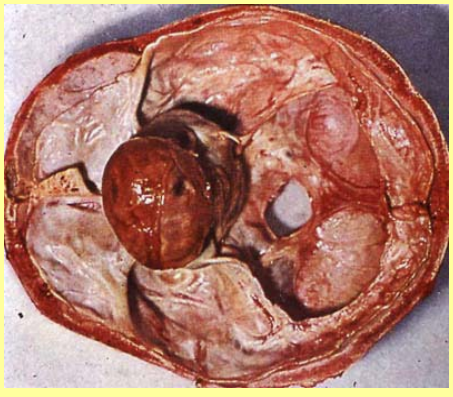


- *While each specific type of hormone secreting cell exhibits some characteristic morphological features, a given cells can only be unequivocally identified through the use immunocytochemical staining procedures*

CHROMOPHOBES: (50%)



- small round pale staining cells with relatively little cytoplasm.
- These cells appear to be <u>non-secretory</u>
- At the EM level they exhibit: few specific staining granules
- thought to represent a degranulated phase of the secretory epithelial cells

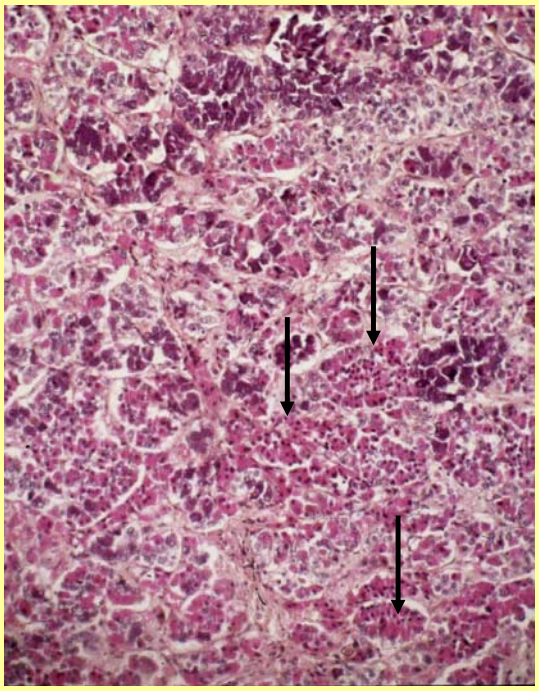


Clinically:

- Tumors of these cells are common and result in destruction of surrounding pituitary tissue and decreased activity of the hormone producing cells.

CHROMOPHILS: (50%)

- Larger than chromophobes, these cell can be broken down into 2 classes;
  Acidophils and ***Basophils*** according to the affinity of their specific granules for acidic or basic dyes.

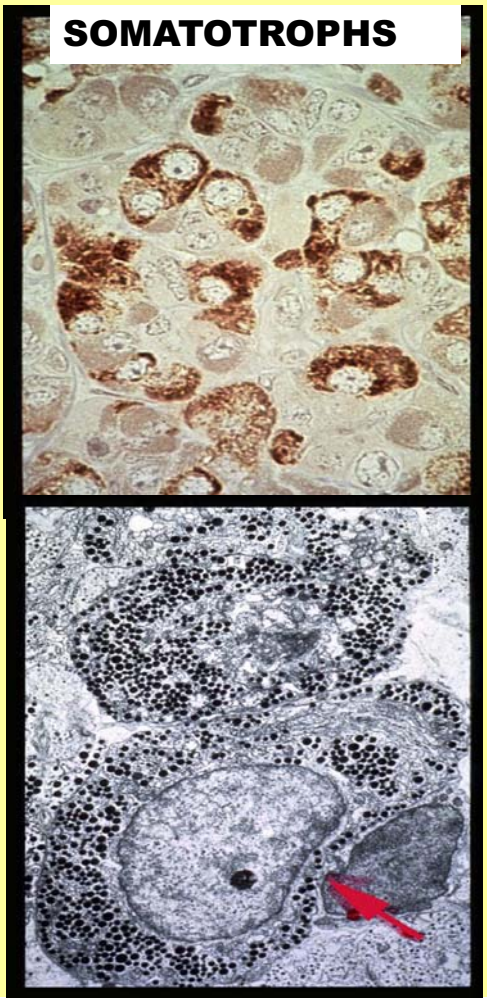


Acidophils: (α cells, approx 40%)

- Large densely staining cells
- cytoplasm packed with small specific granules (acidophilic)
- 2 types of acidophils.
  somatotrophs – mammotrophs
- (ACIDOPHIL SUBTYPES ARE NOT READILY DISTINGUISHABLE WITHOUT IMMUNOCYTOCHEMICAL STAINING)

Somatotrophs:

- spherical to ovoid shape
- centrally located nucleus
- numerous large (350nm) secretory granules which contain
- ***Growth Hormone*** or ***Somatotrophin.***



Growth Hormone:

- (191 amino acids; MW= 21,500)

protein hormone that

1. stimulates chondrocyte growth
2. stimulates cartilage matrix secretion in developing bones.

- **deficiency of GH during development**
  Long bones do not grow
  ►► *pituitary dwarfism*

Pituitary Dwarfism

- **overproduction of GH <u>during development</u> (GH secreting tumors)**
  prolongs bone growth into adulthood = individuals of enormous stature
  ►► *pituitary giantism*

Pituitary Giantism

- **overproduction of GH <u>in adulthood</u>**
  (after closure of the epiphyseal plate)

results in increased bone production and overgrowth in the extremities =
►► *acromegaly*

Acromegaly

In addition to direct effects on target tissues

- **Growth Hormone also regulates the release of other growth promoting compounds in the body. One such class of compounds is the Somatomedins.**
- **These are "insulin-like" growth factors produced in the liver.**
- **The release of Somatomedins from the liver appears to be Growth Hormone dependent.**
- **Somatomedins act to:**
  - **stimulate cartilage growth**
  - **stimulate mitosis**
  - **may be play a role in wound healing**

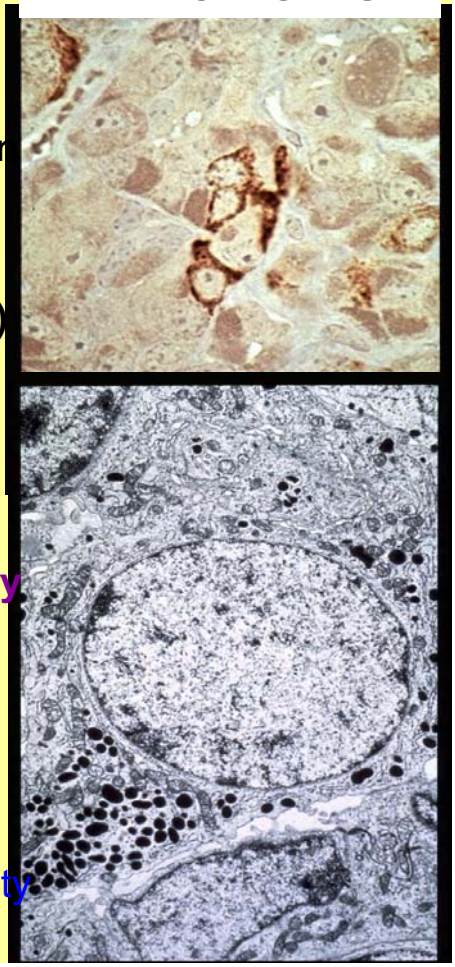
Mammotrophs:

- small irregularly shaped cells -- concentrated in the posterolateral portion of the Pars Distalis – 200nm cytoplasmic granules which contain ***PROLACTIN***
- ***Prolactin:*** (198 amino acids; MW= 22,000)

1. stimulates and maintains the production of milk in the secretory epithelium of the mammary glands
2. maintains the corpora luteum of the ovary to stimulate progesterone secretion

- Hyperplasia of mammotrophs occurs during pregnancy and the cytoplasmic secretory granule increase in size
- In males excess prolactin is linked to infertility

MAMMOTROPHS

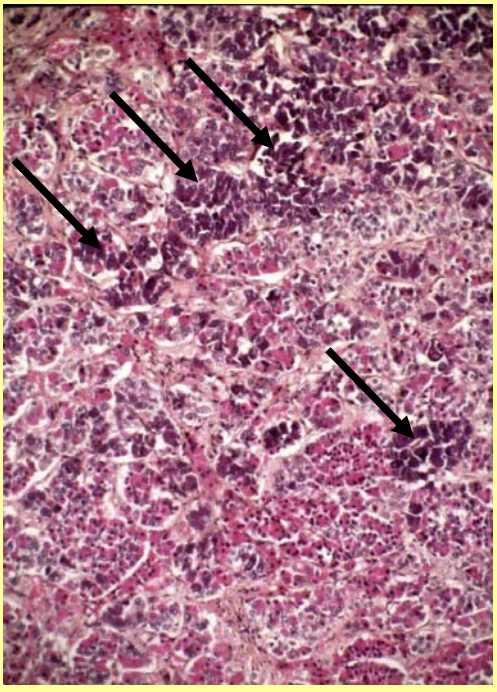


Basophils: (ß cells, approx 10%)

- typically larger than acidophils
- cytoplasmic granules are smaller and less numerous than acidophils

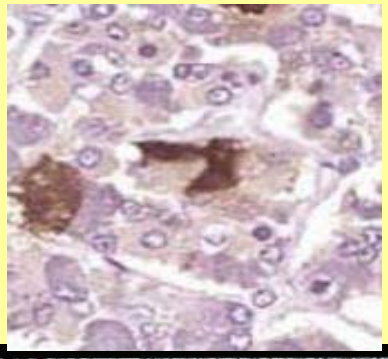
there are 3 classes of basophils (distinguished immunocytochemically)

1. Thyrotrophs
2. Gonadotrophs
3. Corticotrophs



Thyrotrophs:

- **angular cells with small (100-150nm) secretory granules which contain the glycoprotein hormone *THYROID STIMULATING HORMONE (TSH)* (201 amino acids; MW= 28,000)**



- **Cells are scattered throughout the parenchyma usually some distance from sinusoids.**

- **TSH stimulates the biosynthesis & release of thyroxine and triiodothyronine (T4 and T3) from the thyroid gland.**

TSH secretion is under negative feedback control through systemic levels in the blood.

Loss of plasma TSH (hypophysectomy) **----> thyroid gland atrophy**

increased plasma TSH (pituitary tumor) **---> hyperthyroidism**

loss of T3 T4 (Thyroidectomy) **----> increase in Thyrotrophs increased TSH release**

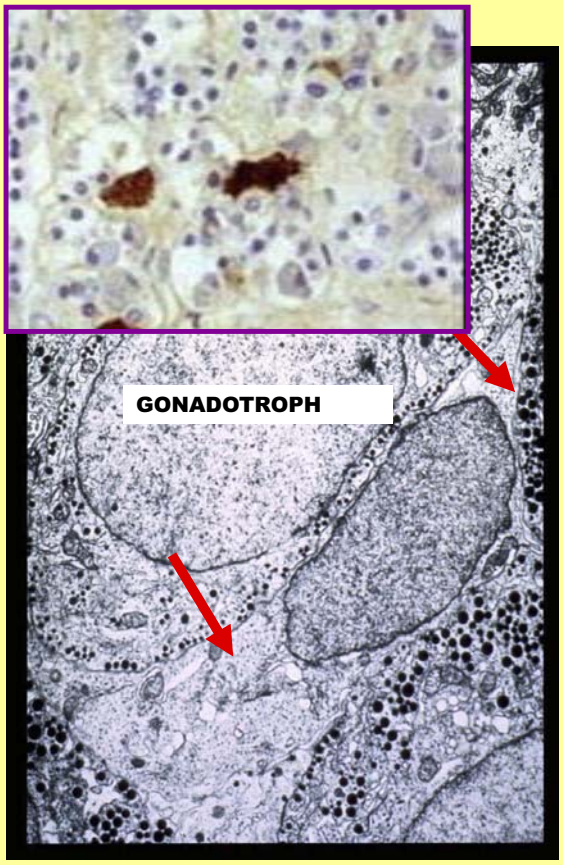
Gonadotrophs:

- fusiform cells w/ eccentric nucleus -- contain varying sized secretory granule ranging from 200-400nm
- gonadotrophs are usually located immediately adjacent to sinusoid

gonadotrophs produce 2 hormones:

-- FOLLICLE STIMULATING HORMONE (FSH)

-- LEUTINIZING HORMONE (LH)



1. ***Follicle Stimulating Hormone:***
   (204 amino acids; MW= 29,000)

   Females **- promotes the growth of ovarian follicles**

   Males **- promotes spermatogenesis by stimulating synthesis "androgen binding protein" in Sertoli cells**

2. ***Leutinizing Hormone*****:**

(204 amino acids; MW= 29,000)

Females:

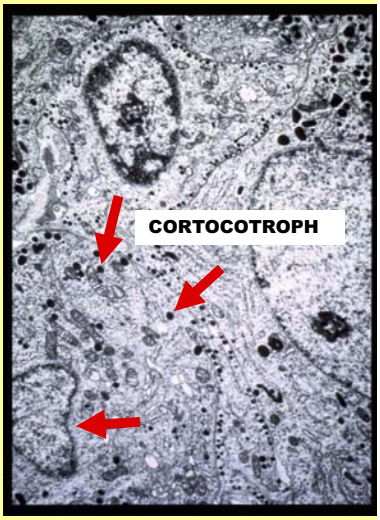
- **promotes ovulation and the maturation of the Corpora Leutea**
- **stimulates progesterone secretion from Corpora Leutea**

Males:

- **Maintains Leydig cells of the testis and stimulates androgen secretion from these cells.**

Corticotrophs: Large ovoid cells w/ eccentric often indented nucleus - contain scattered 200nm secretory granules.

- Produce a prohormone ***PRO-OPIOMALANOCORTIN*** a (285 amino acids) which is cleaved into several smaller peptides.



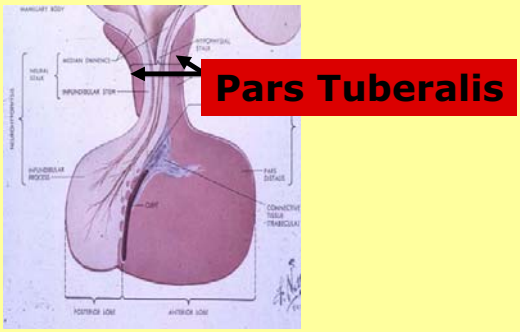
1. ***Adrenocorticotropic Hormone***: a 39 AA peptide (MW= 4500) - stimulates the release of glucocorticoids from the adrenal cortex

2. ***Beta-Endorphin***: small opiate-like peptide, involved in the pain system

3. ***Melanocyte Stimulating Hormone***: stimulates melanin synthesis in malanocytes.

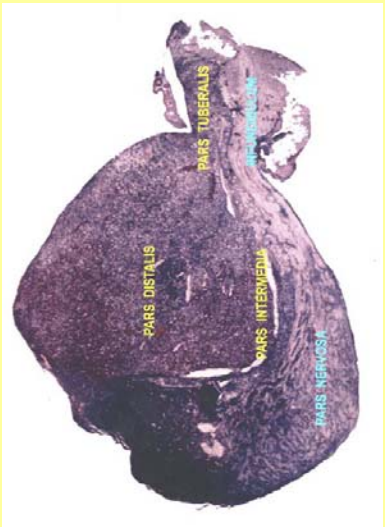
4. ***Beta- Lipotropin***: function in humans unknown (may stimulate lipolysis)

PARS TUBERALIS:



Form a 30-60 µm thick collar of cells wrapped around the infundibular stalk.

Cells are arranged in short longitudinally oriented cords or clumps in close association with capillaries.



The vasculature of the **hypothalamo-hypophyseal portal system** courses through the pars tuberalis on the way to the pars distalis.

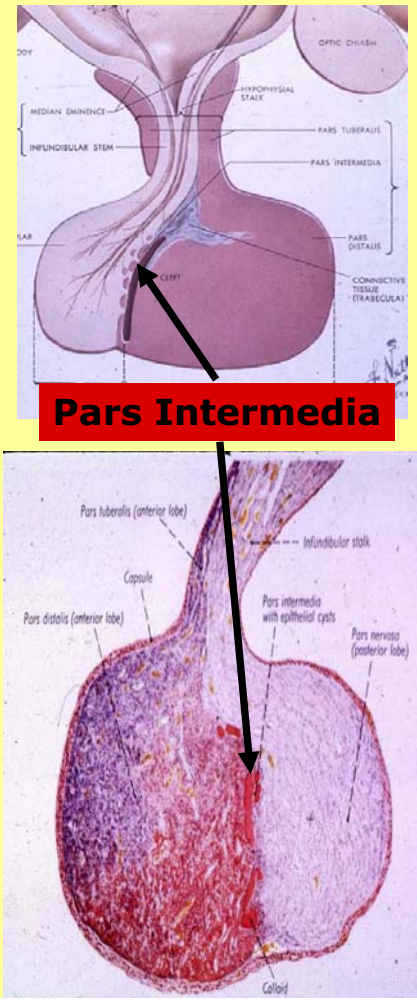
The pars tuberalis contains primarily chromophils cells, mostly "**gonadotrophs**".

PARS INTERMEDIA:

In lower mammals this area represents a partition of basophilic cells dividing the anterior and posterior lobes of the pituitary.

The partition which makes up about 20% of the pitiutary, is marked by an indentation known as "Rathke's Cleft".

In adult humans the pars intermedia is rudimentary, composed of a thin layer of mostly chromophobic cells surrounding aggregates of colloid filled follicles called "Rathke's Cysts".



- Some basophils are present in the human pars intermedia.
- The hormonal secretions of these cells are not entirely clear.
- There appears to be some production of
- - malanocyte stimulating hormone
  - low level of ACTH
- There is often a developmental remnant of Rathke's cleft present in adults humans.

NEUROENDOCRINE LINK OF THE ANTERIOR PITUITARY GLAND:

- Regulation of hormone release from secretory cells in the Pars Distalis is controlled by a complex "neuroendocrine link".
- Specific peptides called "releasing factors" have been identified which modulate the release of hormones from anterior pituitary cells.

- These release modulating peptides are produced by neurons in the basal hypothalamus and are known as *"hypothalamic hypophysiotropic peptides"*
- Each anterior pituitary hormone has its own associated "release promoting peptide" in the hypothalamus, and in at least two instances a specific "release inhibiting peptide".

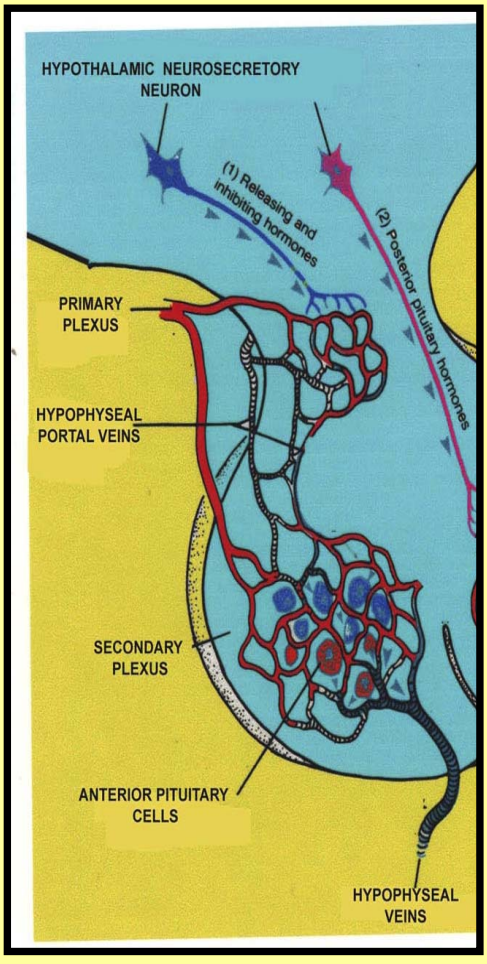


Table 22-2 The Releasing and Inhibiting Hormones and Factors Produced by the Hypothalamus

Anterior Pituitary Hormone	Hypothalamic Releasing Hormone	Hypothalamic Inhibiting Hormone
Growth hormone (GH) or somatotrophin (STH)	Growth hormone-releasing hormone (GRH) or somatotrophin-releasing hormone (SRH)	Growth hormone-inhibiting hormone (GIH), somatotrophin-release-inhibiting hormone (SRIH), or somatostatin
Prolactin (PRL) or lactogenic hormone (LTH)	Prolactin-releasing hormone (PRH)	Prolactin-inhibiting hormone (PIH)
Thyroid-stimulating hormone or thyrotrophin (TSH)	Thyroid-stimulating hormone-releasing hormone or thyrotrophin-releasing hormone (TRH)	
Follicle-stimulating hormone (FSH)	Gonadotrophin-releasing hormone (GnRH, sometimes called LHRH)	
Luteinizing hormone (LH)	Gonadotrophin-releasing hormone (GnRH, sometimes called LHRH)	
Adrenocorticotrophic hormone or corticotrophin (ACTH)	Corticotrophin-releasing hormone (CRH)	
Melanocyte-stimulating hormone (MSH)	Melanocyte-stimulating hormone-releasing factor (MRF)	Melanocyte-stimulating hormone-inhibiting factor (MIF)

The hypothalamic hypophysiotropic peptides are <u>produced in specific hypothalamic regions</u> :

- **preoptic nucleus**
- **paraventricular nucleus**
- **arcuate nucleus**
- **suprachiasmatic**

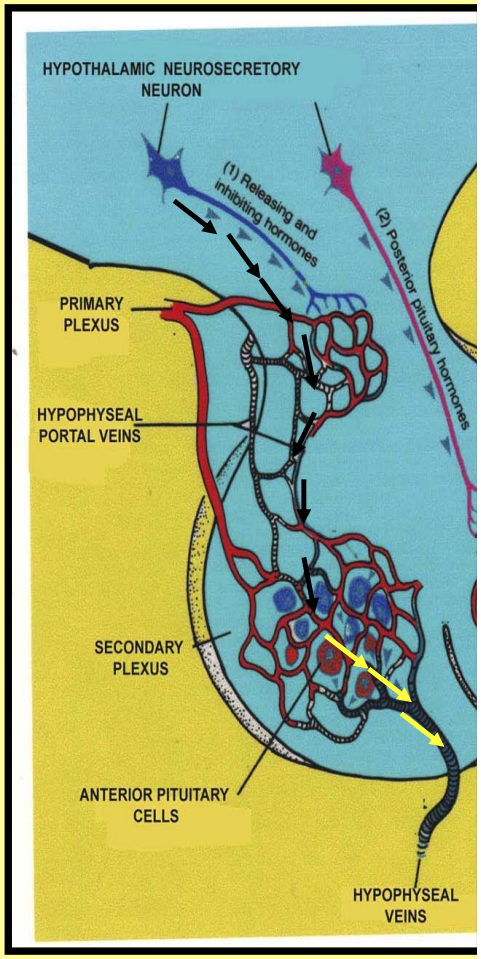
- **The cells in the hypothalamus which produce and secrete these hypophysiotropic peptides are <u>small neurons</u>, whose <u>unmyelinated</u>, slowly conducting axons terminate on fenestrated capillaries in the "primary plexus".**

- **Secretion of these regulatory peptides can be influenced by <u>both neural and hormonal signals</u>.**

- **FOLLOWING THE RELEASE OF THESE PEPTIDES INTO THE FENESTRATED CAPILLARIES OF THE PRIMARY PLEXUS OF THE MEDIAN EMINENCE.**

- **THEY ARE CARRIED VIA THE PORTAL VESSELS TO THE SECONDARY PLEXUS IN THE ANTERIOR LOBE WHERE THEY STIMULATE (or inhibit) ADENOHYPOPHYSEAL CELLS TO SECRETE THEIR DESIGNATED HORMONE.**

- **This unique anatomical association between the brain and the endocrine organs (neuroendocrine link) provides and important link between these two vital communicating and organizing systems of the body.**



THE NEUROHYPOPHYSIS

- **Consists of the Pars Nervosa, the Median Eminence of the Tuber Cinereum and the Infundibular Stalk which connects the pituitary gland to the hypothalamus .**

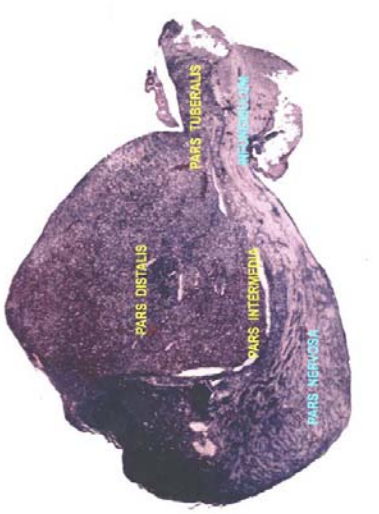
Pars Nervosa: **(posterior lobe)**

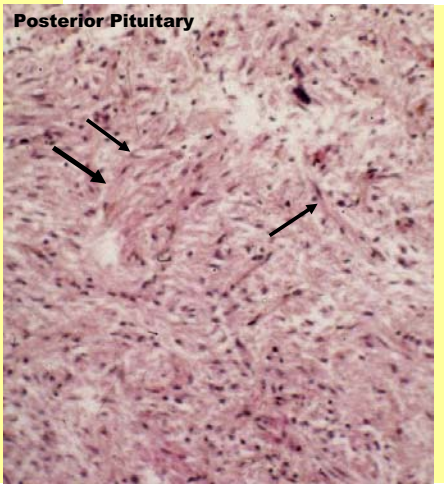
- **The pars Nervosa or "posterior pituitary" consists of three elements**

1. **A dense capillary plexus**

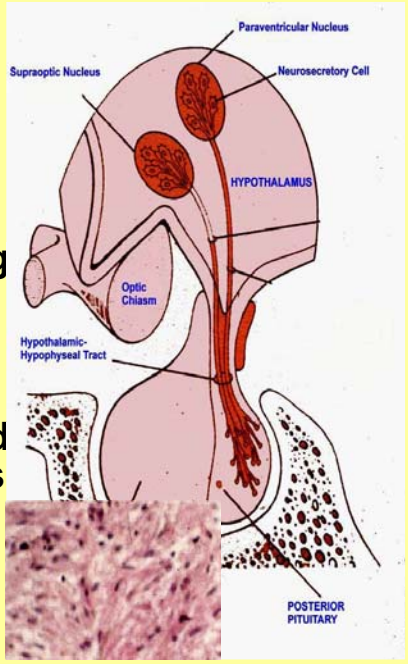
2. **Highly branched non-secretory, glial-like cells called Pituicytes, whose processes end in close association to capillaries. These are thought to serve a nutritive function similar to glial cells in the CNS.**

3. **50,000- 100,000 unmyelinated axons of neurosecretory cells arising from the supraoptic and paraventricular regions of the hypothalamus.**





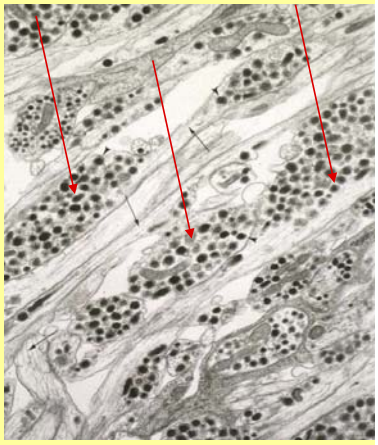
Unlike the Adenohypophysis the posterior lobe does not contain secretory epithelial cells.



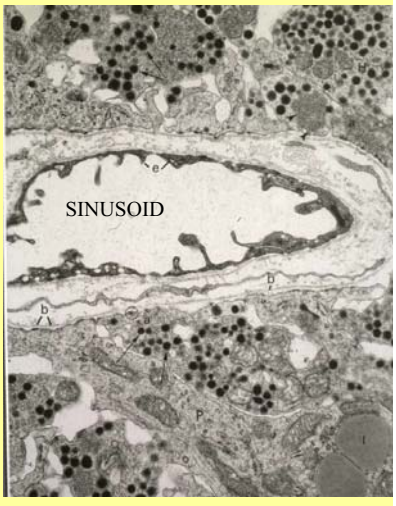
- Hormones are delivered to this gland along the axons of neurosecretory cells in the hypothalamus.
- Descending axons from the supraoptic and paraventricular nuclei of the hypothalamus gather in the infundibulum collect to form a tract called the hypothalamic-hypophyseal tract which terminates on the capillary plexus of the posterior lobe.
- The terminals of these axons are similar to those of other neurons, except that they do not form synapses with other neurons.

Instead they terminate near fenestrated capillaries, where their vesicle bound hormones are secreted via exocytosis.

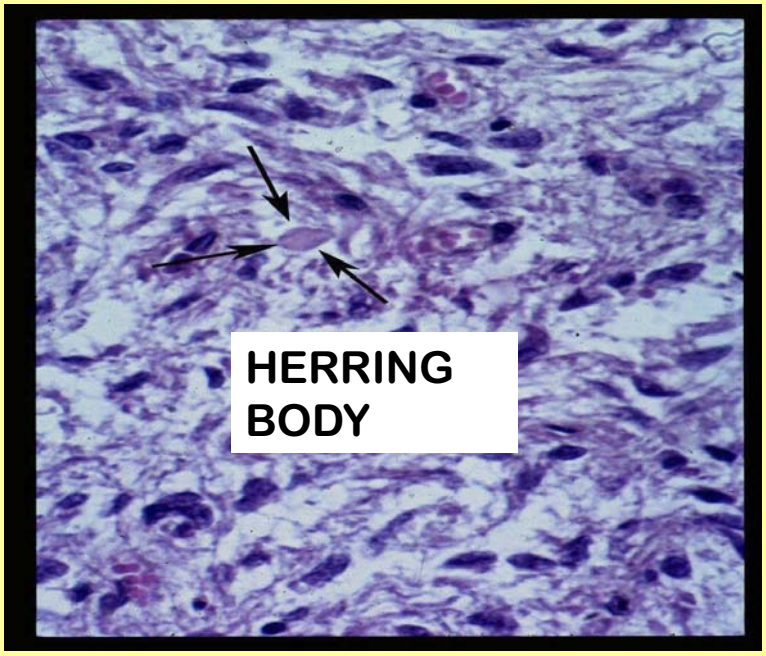
AXON TERMINALS w/ GRANULES



- Hormones are bound to a carrier protein, "Neurophysin" and shipped via axoplasmic transport from the soma to the axon terminals.
- release of hormones at the terminals is signaled by neural impulses traveling down these axons to their terminals.



- **Dense aggregations of vesicle bound hormones cause dilations of the axon terminals called Herring Bodies which can be seen in LM.**



Hormones of the Neurohypophysis

Two major peptide hormones are secreted in the neurohypophysis. These are produces by separate populations of hypothalamic neurosecretory cells:

Oxytocin -- Vasopressin

Oxytocin:

9 amino acid peptide produced primarily in the paraventricular nucleus of the hypothalamus

A. induces peristaltic contractions of uterine smooth muscle to facilitate parturition

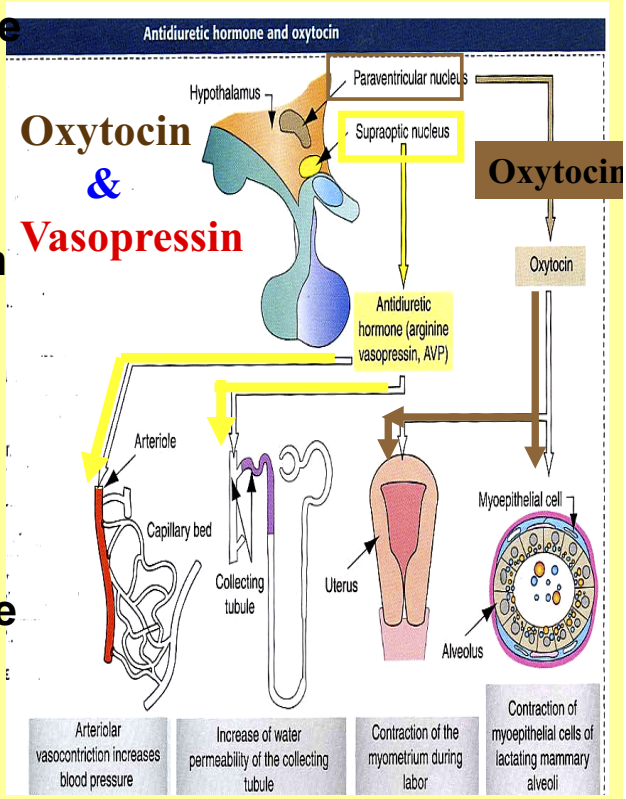
B. induces contraction of myoepithelial cells of the mammary gland resulting in excretion of milk from the secretory alveoli

Vasopressin: (Antidiuretic Hormone)

- also a 9 amino acid peptide produced primarily in the supraoptic nucleus

A. promotes water resorption through the collecting tubules of the kidney

B. Increases blood pressure by promoting Contraction of vascular smooth muscle resulting in increased peripheral resistance



ENDOCRINE FEEDBACK REGULATION

- Most endocrine glands are components of complex homeostatic feedback loops.
- hormones release by target cell activity act back somewhere in the system to accelerate or retard further hormone production and secretion.

Feedback can be:

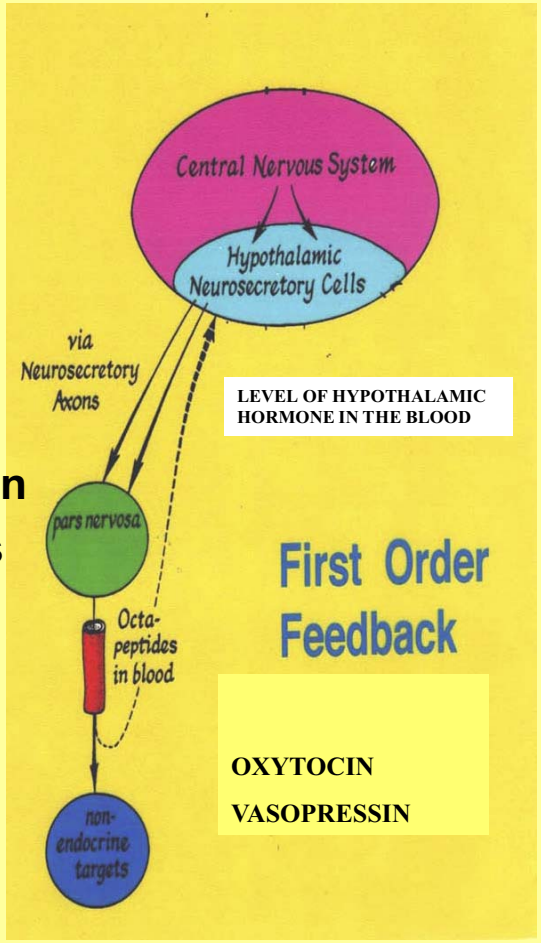
Negative - output of target cells decreases hormone production

Positive - output of target cell increases hormone production

- feedback loops have 3 orders of complexity depending on the location and source of the hormone that regulates the feedback to the pituitary.

First Order:

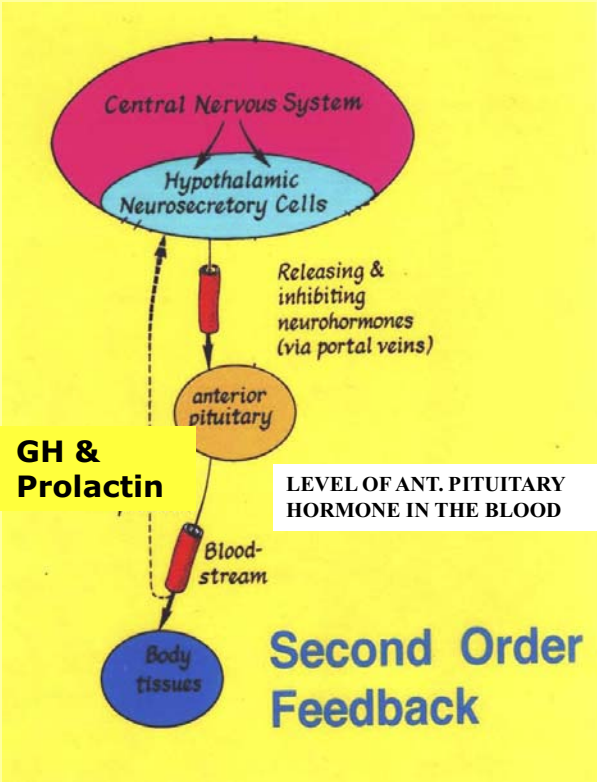
- Neurohypophyseal Hormone acts on non-endocrine target organ (oxytocin, vasopressin).
- the levels of this hormone or the products of the target organ feed back to the hypothalamus to regulate further release of hormone from this structure.



Second Order:

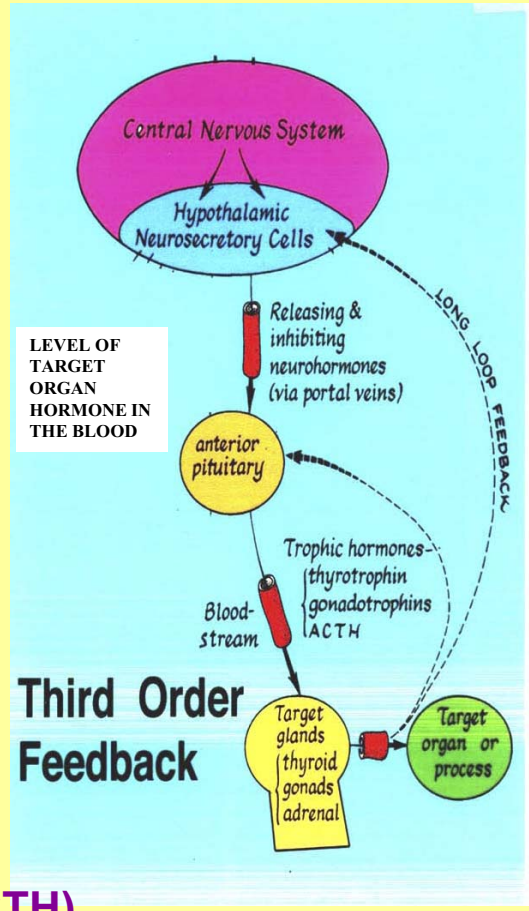
- Hypothalamic releasing Factor stimulates release of <u>Pituitary Hormone</u>
- Which act on peripheral target tissues.
- Plasma level of the <u>Pituitary Hormone</u> feeds back to the Hypothalamus or Pituitary to regulate further hormone release.

(Growth Hormone, Prolactin)



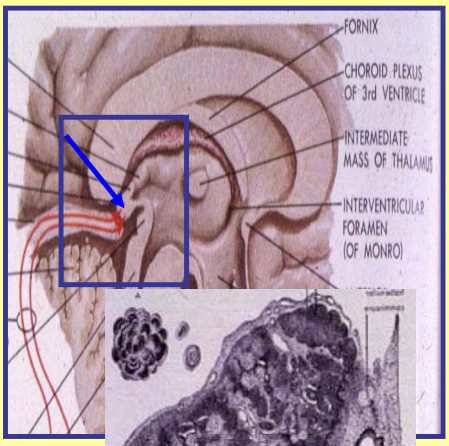
Third Order:

- **Hypothalamic releasing factor stimulates the secretion of a pituitary hormone**
- **secretion of the pituitary hormone stimulates peripheral target *endocrine* organ to secrete its own peripheral hormone**
- **level of peripheral target organ hormone feeds back to the pituitary or hypothalamus to regulate further hormone release via their specific hypothalamic releasing factor.**

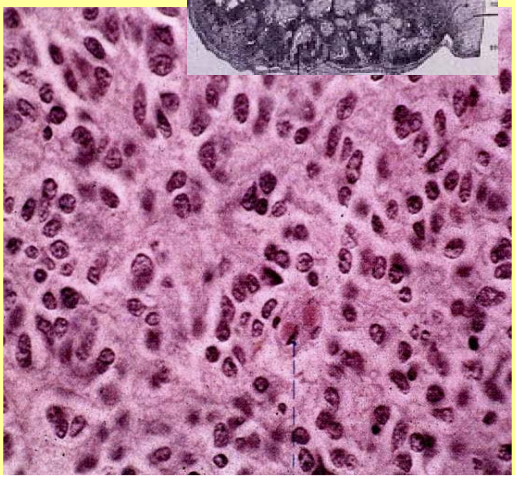


(Thyroid Stimulating Hormone, ACTH)

PINEAL GLAND: (Epiphysis Cerebri)



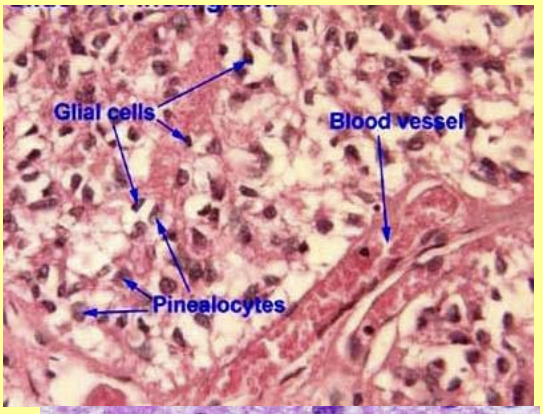
- **Flattened conical gland attached to the midline of the superior surface of the diencephalon of the CNS**
- **Encapsulated by the connective tissue Pia of the CNS which penetrate the parenchyma as trabeculae.**
- **Populated by 2 major cell types =**

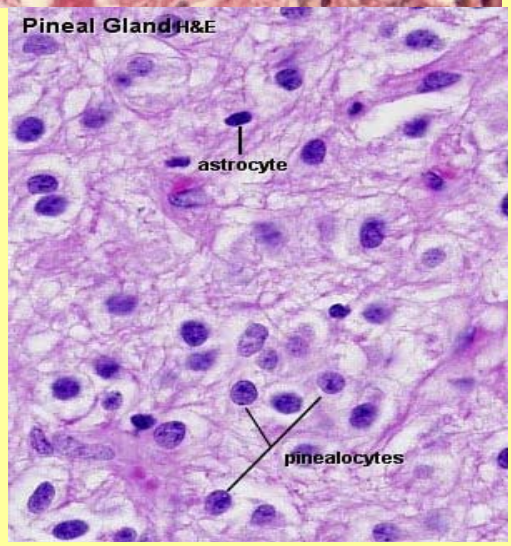


PINEALOCYTES --- GLIAL CELLS

Pinealocytes

- Basophilic cytoplasm w/ long cytoplasmic processes which end in bulb-like expansion in close proximity to capillaries.
- These extensions exhibit small dense-core vesicles similar to those seen in catacholaminergic neurons which appear to be exocytosed into the capillaries.
- large oval nucleus and clearly distinguishable nucleoli





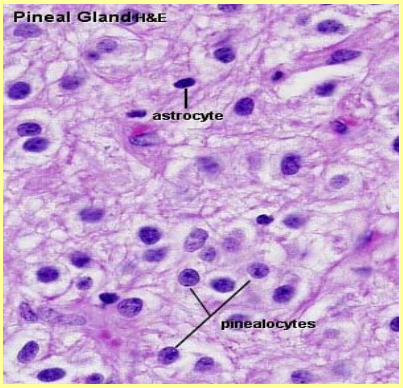
Pinealocytes produce **MELATONIN** which they synthesize from **SEROTONIN**.

The physiological functions of Melatonin are not well understood.

- it appears to cause **retention of pigment granules in melanophores in** the skin and thus has an effect opposite that of MSH
- It also exhibits **anti-gonadotrophic effects and may inhibit FSH and LH activity**. This may be important in seasonal breeding animals to coordinate reproduction with seasonal variations in day length
- appear to be a powerful free radical scavenger and anti-oxidant

- released during the dark cycle (inhibited by light)
- Melatonoin may inhibit the growth and metastasis of some tumors
- Overproduction of Melatonin may be involved in "Seasonal Affective Disorder"
- appears to be involved in regulating bio-rhythyms and sleep/wake cycle

Glial Cells: (*Interstitial Cells*)



- Resemble astrocytes of the CNS both structurally and immunocytochemically.

The pineal gland characteristically contains small aggregates of calcium phosphate and calcium carbonate known as ***Brain Sand.***

- These are radiopaque and were used (before the days of MRI) clinically to indicate brain compression and space-occupying lesions of the CNS